CLAIMS

1. A compound of the formula

$$R^3$$
 N
 K
 G
 R^5

or a pharmaceutically acceptable salt thereof, wherein the dashed lines represent optional double bonds;

A is nitrogen or CR7:

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B is $-NR^1R^2$, $-CR^1R^2R^{10}$ $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$;

J and K are each independently nitrogen or carbon and both J and K are not nitrogens;

D and E are each selected, independently, from nitrogen, CR⁴, C=O, C=S, sulfur, oxygen, CR⁴R⁶ and NR⁸;

G is nitrogen or carbon;

the ring containing D, E, G, K, and J in formula I may be a saturated or unsaturated 5-membered ring and may optionally contain one or two double bonds and may optionally contain from one to three heteroatoms in the ring and may optionally have one or two C=O or C=S groups;

 R^1 is C_1 - C_6 alkyl optionally substituted with one or two substituents independently selected from hydroxy, fluoro, chloro, bromo, iodo, -O-(C_1 - C_4 alkyl), CF_3 , -C(=O)O-(C_1 - C_4 alkyl), -OC(=O)(C_1 - C_4 alkyl), -OC(=O)N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), -NHCO(C_1 - C_4 alkyl), -COOH, -COO(C_1 - C_4 alkyl), -CONH(C_1 - C_4 alkyl), -CON(C_1 - C_4 alkyl)(C_1 - C_4 alkyl), -S(C_1 - C_4 alkyl), -SO₂(C_1 - C_4 alkyl), -SO₂NH(C_1 - C_4 alkyl) and -SO₂N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), wherein each of the C_1 - C_4 alkyl groups in the foregoing R^1 groups may optionally contain one or two double or triple bonds;

 R^2 is C_1 - C_{12} alkyl which may optionally contain from one to three double or triple bonds, aryl or $(C_1$ - C_4 alkylene)aryl, wherein said aryl and the aryl moiety of said $(C_1$ - C_4 alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; C_3 - C_8 cycloalkyl or $(C_1$ - C_6 alkylene) $(C_3$ - C_8 cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said $(C_1$ - C_6 alkylene) $(C_3$ - C_8 cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, C_1 - C_4

alkyl, benzyl and C_1 - C_4 alkanoyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C_1 - C_4 alkyl, or with one substituent selected from bromo, iodo, C_1 - C_6 alkoxy, $-OC(=O)(C_1$ - C_6 alkyl), $-OC(=O)N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-S(C_1$ - C_6 alkyl), amino, $-NH(C_1$ - C_2 alkyl), $-N(C_1$ - C_2 alkyl)(C_1 - C_4 alkyl), $-N(C_1$ - C_4 alkyl), $-NHCO(C_1$ - C_4 alkyl), $-CON(C_1$ - C_4 alkyl), $-CON(C_1$ - C_4 alkyl), $-SN_2$ - $-SO(C_1$ - $-SN_4$ alkyl), $-SN_2$ - $-SN_4$ alkyl), $-SN_2$ - $-SN_4$ alkyl), $-SN_2$ - $-SN_4$ alkyl), $-SN_2$ - $-SN_4$ - $-SN_4$ alkyl), $-SN_2$ - $-SN_4$ -

-NR¹R² or CR¹R²R¹⁰ may form a saturated 3 to 8 membered carbocyclic ring which may optionally contain from one to three double bonds and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ³ wherein Z³ is hydrogen, C₁-C₄ alkyl, benzyl or C₁-C₄ alkanoyl;

 R^3 is hydrogen, C_1 - C_4 alkyl, -O(C_1 - C_4 alkyl), chloro, fluoro, bromo, iodo, (C_1 - C_2 alkylene)-O-(C_1 - C_2 alkyl), (C_1 - C_2 alkylene)-OH, or -S(C_1 - C_4 alkyl);

each R^4 is, independently, hydrogen, (C₁-C₆ alkyl), fluoro, chloro, bromo, iodo, hydroxy, cyano, amino, (C₁-C₂ alkylene)-OH, CF₃, CH₂SCH₃, nitro, -O(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₄ alkyl), -C(C₁-C₄ alkyl), -C(=O)H or -C(=O)O(C₁-C₄alkyl);

R⁶ is hydrogen, methyl or ethyl;

R⁸ is hydrogen or C₁-C₄ alkyl:

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 R^5 is phenyl, pyridyl, pyrazinyl, pyrimidyl, pyridazinyl and wherein each of the foregoing R^5 groups is substituted with from one to four substituents R^{13} wherein one to three of said substituents may be selected, independently, from fluoro, chloro, C_1 - C_6 alkyl and -O(C_1 - C_6 alkyl) and one of said substituents may be selected from bromo, iodo, formyl, OH, (C_1 - C_4 alkylene)-OH, (C_1 - C_4 alkylene)-O-(C_1 - C_2 alkyl), -CN, -CF $_3$, -NO $_2$, -NH $_2$, -NH(C_1 - C_4 alkyl), -N(C_1 - C_2 alkyl)(C_1 - C_6 alkyl), -OCO(C_1 - C_4 alkyl), (C_1 - C_4 alkylene)-O-(C_1 - C_4 alkyl), -S(C_1 - C_6 alkyl), (C_1 - C_4 alkyl), -C(=O)(C_1 - C_4 alkyl), -C(=O)(C_1 - C_4 alkyl), -SO $_2$ NH(C_1 - C_4 alkyl), -SO $_2$ NH(C_1 - C_4 alkyl), and wherein each of the C_1 - C_4 alkyl and C_1 - C_6 alkyl moieties in the foregoing R^5 groups may optionally have one or two double bonds;

 R^7 is hydrogen, C_1 - C_4 alkyl, halo (<u>e.g.</u>, chloro, fluoro, iodo or bromo), hydroxy, -O(C_1 - C_4 alkyl), -C(=O)(C_1 - C_4 alkyl), -C(=O)(C_1 - C_4 alkyl), -O(E_3 , -C E_3 , -C E_4 -OH or -CH₂O(E_1 - E_4 alkyl);

R¹⁰ is hydrogen, hydroxy, methoxy or fluoro;

R¹¹ is hydrogen or C₁-C₄ alkyl; and

with the proviso that: a) when both J and K are carbons and D is CR⁴ and E is nitrogen, then G can not be nitrogen; (b) when both J and K are carbons and D and G are nitrogens, then E can not be CR⁴ or C=O or C=S; (c) when both J and K are carbons and D and E are carbons.

then G can not be nitrogen; (d) when G is carbon, it must be double banded to E; and (e) in the ring containing J, K, D, E and G, there can not be two double bonds adjacent to each other;

and the pharmaceutically acceptable salts of such compounds.

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- 2. Compounds according to claim 1 wherein B is -NR 1 R 2 , -NHCHR 1 R 2 , -OCHR 1 R 2 and R 1 is C $_1$ -C $_6$ alkyl, which may optionally be substituted with one fluoro, or C $_1$ -C $_4$ alkoxy group and which may optionally contain one double or triple bond; and R 2 is C $_1$ -C $_4$ alkyl or (C $_1$ -C $_2$ alkyl)-CO-(C $_1$ -C $_2$ alkyl) which may optionally contain one double or triple bond.
- 3. Compounds according to claim 1, wherein B is -CHR 1 R 2 , -NR 1 R 2 , -NHCHR 1 R 2 , -OCHR 1 R 2 , -SCHR 1 R 2 ; and R 1 is C $_1$ -C $_6$ alkyl, which may optionally be substituted with one hydroxy, fluoro, CF $_3$, cyclopropyl or C $_1$ -C $_4$ alkoxy group and which may optionally contain one double or triple bond; and R 2 is benzyl or C $_1$ -C $_6$ alkyl, which may optionally contain one double or triple bond, wherein said C $_1$ -C $_6$ alkyl and the phenyl moiety of said benzyl may optionally be substituted with one fluoro, hydroxy, CF $_3$, cyclopropyl, C $_1$ -C $_2$ alkyl, C $_1$ -C $_2$ alkoxy or chloro group.
 - 4. Compounds according to claim 1 wherein R³ is methyl.
- 5. Compounds according to claim 1 wherein R⁴, R⁶, R⁸, R⁹, and R¹² are hydrogen or methyl.
- 6. Compounds according to claim 1 wherein R^5 is di- or tri-substituted phenyl in which the two or three substitutents are independently selected from C_1 - C_4 alkyl, O- $(C_1$ - C_4 alkyl), $(C_1$ - C_4 alkylene)-O- $(C_1$ - C_4 alkyl), CF_3 , OCF_3 , CHO, $(C_1$ - C_4 alkylene)-OH, cyano, chloro, fluoro, bromo and iodo, wherein each of the forgoing $(C_1$ - C_4) alkyl groups may optionally contain one double or triple bond.
- 7. Compounds 1 wherein R^3 is methyl, ethyl, chloro or methoxy; and each of R^4 , R^6 , R^8 , R^9 , and R^{12} is, independently, hydrogen, methyl or ethyl.
- 8. Compounds wherein R^5 is di- or tri-substituted pyridyl, or pyrimidyl in which the two or three substitutents are independently selected from C_1 - C_4 alkyl, O- $(C_1$ - C_4 alkyl), $(C_1$ - C_4 alkylene)-O- $(C_1$ - C_4 alkyl), $(C_1$ - C_4 alkylene)- $(C_1$ - $(C_4$ alkyl), $(C_1$ - $(C_4$ alkylene)- $(C_1$ -(
 - 9. Compounds according to claim 1 wherein A is N, CH or CCH₃.
- 10. Compounds according to claim 1 wherein A is CH, J and K are carbon and D, E, and G are nitrogen.
- 11. Compounds according to claim 1 wherein J and D are nitrogen, and K and G are carbon, and E is CH, CCH₃ or CC₂H₅.
- 12. Compounds according to claim 1 wherein J and K are carbon, and D₋₋EG isO-C(CH₃)=C, O-CH=C, S-C(CH₃)=C, S-CH=C, N(CH₃)-C(CH₃)=C, NHC(CH₃)=C, NHC(CH₃)-CH=C, O-N=C, S-N=C, N(CH₃)-N=C, O-CH₂N or S-CH₂N.

- 13. A compound according to claim 1 wherein B is -CHR¹R², -NCHR¹R² or -OCHR¹R², and the CHR¹R² group of B is a cyclopentane ring, a tetrahydrofuran ring or a tetrahydrothienyl ring.
- 14. A compound according to claim 1 wherein the NR¹R² group of B is a five membered saturated or unsaturated heterocyclic ring.

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- 15. A compound according to claim 14 wherein the NR¹R² is a pyrrolo ring, a pyrrolidino ring, a thiazolidino ring or a morpholino ring.
- 16. A pharmaceutical composition for the treatment, prevention or inhibition of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, or (b) a disorder selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent, . depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stressinduced fever; human immunodeficiency virus (HIV) infections; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies and addictions (e.g., dependencies on alcohol, cocaine, heroin, benzodiazepines, or other drugs); drug and alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiarrhetic hormone (ADH); obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage (e.g., cerebral ischemia such as cerebral hippocampal ischemia); excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions (e.g., porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, and dysfunctions induced by confinement in chickens, sheering stress in sheep or human-animal interaction related stress in dogs); muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; and hypoglycemia in a mammal, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder, and a pharmaceutically acceptable carrier.
- 17. A method for the treatment, prevention or inhibition of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, or (b) a disorder selected from inflammatory

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disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus (HIV) infections; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies and addictions (e.g., dependencies on alcohol, cocaine, heroin, benzodiazepines, or other drugs); drug and alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiarrhetic hormone (ADH); obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage (e.g., cerebral ischemia such as cerebral hippocampal ischemia); excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions (e.g., porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, and dysfunctions induced by confinement in chickens, sheering stress in sheep or human-animal interaction related stress in dogs); muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; and hypoglycemia in a mammal, comprising administering to a subject in need of said treatment an amount of a compound according to claim 1, that is effective in treating such disorder.

- 18. A method of treating or preventing a disorder or condition, the treatment or prevention of which can be effected or facilitated by inhibiting CRH binding protein in a mammal, comprising administering to said mammal a CRH binding protein inhibiting amount of a compound according to claim 1.
- 19. A pharmaceutical composition for treating or preventing a disorder or condition, the treatment or prevention of which can be effected or facilitated by inhibiting CRH binding protein in a mammal, comprising a CRH binding protein inhibiting amount of a compound according to claim 1 and a pharmaceutically acceptable carrier.
- 20. A compound according to claim 11 or 12 wherein A is N or CH, R³ is methyl and each R⁴, R⁶, R⁸, R⁹ and R¹² is, independently, hydrogen or methyl.
- 21. A compound according to claim 20, wherein R^5 is di- or tri-substituted phenyl, wherein the two or three substitutents are independently selected from C_1 - C_4 alkyl, O- $(C_1$ - C_4 alkyl), $(C_1$ - C_4 alkylene)-O- $(C_1$ - C_4 alkyl), $(C_1$ - C_4 alkylene)- $(C_1$ - $(C_4$ alkyl), $(C_1$ - $(C_4$ alkylene)- $(C_1$ - $(C_4$ alkyl), $(C_1$ - $(C_4$ alkylene)- $(C_1$ - $(C_4$ alkyl), $(C_1$ -

fluoro, bromo and iodo, wherein each of the forgoing (C₁-C₄) alkyl groups may optionally contain one double or triple bond.

22. A compound of the formula

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amine;

amine;

amine;

$$R^3$$
 R^4
 R^5
 R^5
 R^6
 R^6
 R^6
 R^6
 R^6

or

$$\mathbb{R}^3$$
 \mathbb{R}^4
 \mathbb{R}^5

wherein R^3N is C_1 - C_4 alkyl, R^7N is hydrogen, methyl, chloro, bromo, -COOH or -COO(C_1 - C_4 alkyl), T is chloro, bromo, iodo or triflate, R^8 is hydrogen or C_1 - C_4 alkyl and R^4 is hydrogen, (C_1 - C_6 alkyl), fluoro, chloro, bromo, iodo, hydroxy, cyano, amino, (C_1 - C_2 alkylene)-OH, CF_3 , CH_2SCH_3 , nitro, -O(C_1 - C_4 alkyl), -N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), -S(C_1 - C_4 alkyl), -CO(C_1 - C_4 alkyl), -C(=O)H or -C(=O)O(C_1 - C_4 alkyl);

23. A compound according to claim 1 wherein said compound is: 7-(1-ethyl-propoxy)-5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-

(1-Ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-

7-(1-Ethyl-propoxy)-2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidine; [2,5-Dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-ethyl-propyl-

[6-Bromo-5-bromomethyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]-(1-ethyl-propyl)-amine;

(1-Ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]-amine;

[6-Bromo-5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]-(1-ethyl-propyl)-methyl-amine;

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or

7-(1-Ethyl-propoxy)-5-methyl-3-(2,4,6-trimethyl-phényl)-3H-[1,2,3]triazolo[4,5-b]pyridine; 4-(1-Ethyl-propoxy)-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyr imidine;

(<u>+</u>)-2,5-Dimethyl-4-(tetrahydro-furan-3-yloxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo-[3,2-d]pyrimidine;

2, 5- Dimethyl-4-(S)-(tetrahydro-furan-3-yloxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo-[3,2-d] pyrimidine;

2,5-Dimethyl-4-(1-propyl-butoxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;

4-sec-Butylsulfanyl-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine; or a pharmaceutically acceptable salt of such compound.